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Clinical Research

Benefit of Allogeneic Transplantation in Patients Age ≥ 60 Years with Acute Myeloid Leukemia Is Limited to Those in First Complete Remission at Time of Transplant

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A B S T R A C T

We evaluated the impact of age and remission status on 242 consecutive patients who underwent allogeneic hematopoietic cell transplantation for acute myeloid leukemia (AML) in our program between 1999 and 2011. Median age of all patients was 48 years (range, 18 to 71). Based on age and remission status, patients were divided into 4 groups: first complete remission (CR1) age <60 years (n = 116), second complete remission (CR2) age <60 years (n = 78), CR1 age ≥60 years (n = 32), and CR2 age ≥60 years (n = 16). Donors were matched related (n = 155, 64%) or matched unrelated (n = 87, 36%). Median follow-up of survivors was 65 months (range, 12 to 145). In a univariate analysis, 3-year overall survival rates of the 4 groups were 57%, 43%, 39%, and 16% ($P = .003$), respectively. In a multivariable analysis, hazard ratios of nonrelapse mortality and survival were 2.08 ($P = .06$) and 1.52 ($P = .23$), respectively, in patients ≥60 years in CR2 compared with ≥ 60 years in CR1. Although a plateau in survival was observed for patients ≥60 years in CR1 similar to those <60 years in CR1 and CR2, no long-term survivors were seen in patients ≥60 years in CR2. Our data suggest disappointing outcomes in AML patients ≥60 years of age transplanted in CR2. Therefore, if a transplant is indicated, early referral is recommended in patients ≥60 years with AML.

INTRODUCTION

Allogeneic hematopoietic cell transplantation (HCT) offers curative potential in the treatment of patients with acute myeloid leukemia (AML). The advantage of HCT compared with conventional chemotherapy for subgroups of AML patients was previously reviewed [1]. A meta-analysis demonstrated improved survival in patients aged ≤ 60 years with AML in first complete remission (CR1) with intermediate or adverse cytogenetics at diagnosis who underwent HCT compared with those who received conventional chemotherapy [2]. The benefit of HCT for younger patients was recently demonstrated in patients with AML in second complete remission (CR2), who had intermediate- or adverse-risk cytogenetics [3].

The outcomes of younger patients with AML have improved in the last 2 decades. Factors contributing to improved outcomes in younger patients with AML include improvements in supportive care and increased utilization as well as optimization of HCT [4]. Although outcomes of younger patients with AML have improved, no significant improvement has been observed in older patients [5]. A case-controlled study showed improved outcome of patients ages 60 to 70 years treated with HCT compared with chemotherapy alone [6].

In transplant recipients, some studies demonstrated that older age alone did not significantly affect survival post-transplant but remission status did, with a significant advantage for patients transplanted in CR1 [7]. On the contrary, another study showed that remission status did not affect survival of patients with AML post-HCT using reduced-intensity conditioning (RIC); however, this study included patients with a wide range of ages, including younger patients [8]. A Center for International Blood and Marrow Transplant Research study showed that older patients undergoing RIC HCT for AML in CR1 benefit as equally as younger patients [9]. Reports in the literature concerning the benefit of older patients (≥60 years) in CR2 are conflicting. Some studies demonstrated a lack of significant effect of patient age on outcome [10,11], whereas others found that patient age ≥55 years is a predictor of poor survival after HCT for AML in CR2 [12].

We evaluated the impact of age in association with remission status on the outcomes of 242 consecutive patients who underwent HCT for AML in our program from 1999 to 2011. We report that HCT offers a curative potential to AML patients ≥60 years in CR1 similar to younger patients; however, the outcomes in patients ≥60 years in CR2 are disappointing. We also explore the causes for poor outcomes

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in these patients to guide practice improvements for the future.

METHODS

Patients

The study population consisted of 242 consecutive patients aged 18 to 71 years undergoing first allogeneic transplant for AML in CR1 and CR2 from matched related (n = 155) or matched unrelated donors (n = 87) between January 1999 and June 2011 at Princess Margaret Cancer Centre, Toronto, Ontario, Canada. Among these patients, 194 (80%) were age <60 at transplant, and 48 (20%) were age ≥60 years. Data were collected from the Electronic Patient Records of the hospital as well as the Bone Marrow Transplant Program database. The study was approved by the Cancer Registry Data Access Committee and the Research Ethics Board of the University Health Network/Princess Margaret Cancer Centre (REB no. 12-0048-CE).

Data

Data collected and subsequently analyzed involved a number of pretransplant variables, including age, gender, cytogenetic risk at diagnosis, conditioning regimen, hematopoietic progenitor cell source, related or unrelated donor status, and cytomegalovirus serostatus of donor and recipient. Based on age and remission status, patients were divided into 4 groups: CR1 age <60 years, CR2 age <60 years, CR1 age ≥60 years, and CR2 age ≥ 60 years. Cytogenetics at diagnosis was characterized as favorable, intermediate, unfavorable, and unknown risk as previously described [13].

The HCT-comorbidity index was calculated for all transplanted patients retrospectively from the pretransplant investigations and chart review. Comorbidities were analyzed as presenting with either a low-risk (0 to 2) or high-risk score (≥3) [14].

Conditioning Regimens and Graft-versus-Host Disease Prophylaxis

Patients were conditioned either with myeloablative conditioning or RIC regimens. The decision to offer RIC was primarily based on patient age and the presence of significant comorbidities, as previously described [15]. Classification of the intensity of conditioning regimen was based on the Center for International Blood and Marrow Transplant Research suggested criteria [16]. The myeloablative conditioning regimens were subdivided into 2 groups. First, those used from 1999 to 2006 included busulfan 3.2 mg/kg for 4 days and cyclophosphamide 60 mg/kg for 2 days cyclophosphamide 60 mg/kg for 2 days and total body irradiation 12 Gy. Second, since 2006 patients received conditioning with fludarabine 50 mg/m^2 for 4 days, busulfan 3.2 mg/kg for 4 days, and total body irradiation 400 cGy in 2 fractions.

RIC regimens used between 1999 and2006 included combinations of fludarabine 30 mg/m^2 for 4 to 5 days with busulfan 3.2 mg/kg for 2 days or with total body irradiation 200 cGy [17]. Since 2006 patients were conditioned with fludarabine 30 mg/m^2 for 4 days, busulfan 3.2 mg/kg for 2 days, and total body irradiation 200 cGy.

Graft-versus-host disease prophylaxis consisted of cyclosporine A, combined with either methotrexate (15 mg/m^2 on HCT day +1 and 10 mg/m^2 on HCT days +3, +6, and +11; n = 124) or mycophenolate mofetil (given for 28 days post-transplant; n = 60). Serotherapy using low-dose alemtuzumab or antithymocyte globulin was used in combination with cyclosporine A in 58 patients undergoing unrelated donor transplantation.

Definitions of Clinical Endpoints

For the purpose of this study, complete remission (CR) was defined as achievement of a bone marrow with <5% blasts and count recovery. Relapse was defined as ≥5% blasts in a bone marrow aspirate or peripheral blood or the development of extramedullary leukemia after transplant. Overall survival (OS) times were measured from the date of HCT until death from any cause. Alive patients were censored on the date of their last follow-up. Leukemia-free survival (LFS) was defined as the time from transplantation to relapse or death from any cause. Nonrelapse mortality (NRM) was calculated as death without evidence of disease relapse.

Statistical Analysis

Patient demographics and treatment-related outcomes were reported using descriptive statistics. Categorical variables were summarized with counts and percentages. Continuous variables were summarized with means and/or medians with ranges. Data were updated as of June 2012.

Contingency statistics using the chi-square test or Fisher's exact test (as appropriate) were performed for the comparison of distribution of the variables between the four groups defined by CR status/age combination. Analysis of variance was used to compare the continuous outcome age at transplant among the 4 groups.

The main outcome variables of interest were death due to any cause OS, LFS, cumulative incidence of relapse CIR, and cumulative incidence of NRM. OS and LFS were calculated using the Kaplan-Meier product-limit method. The log-rank test was used as a univariate analysis to compare the levels of the 4 groups consisting of age/CR status combination as well as baseline patient characteristics. CIR and NRM were calculated using the competing risk method based on Pepe and Mori's method [18]. The Fine and Gry method for competing risks was used for univariate and multivariable analyses in comparing CIR and NRM.

Because of the small sample size, we performed a limited multivariable analysis using clinically relevant factors. The following factors were analyzed: age/remission status (<60 in CR1, <60 in CR2, ≥60 in CR1, and ≥60 in CR2), donor type (related versus unrelated), conditioning regimen (myeloablative conditioning versus RIC), HCT-comorbidity index score (0 to 2 versus ≥3), and time period of HCT (before or after 2006, which was when different conditioning regimens were used as described previously). Results were considered significant if $P < .05$. Statistical analyses were performed using version 9.2 of the SAS system and user's guide (SAS Institute, Inc., Cary, NC) and R version 2.14.0, the R foundation for statistical computing.

RESULTS

Patient and Transplant Characteristics

Baseline patient, disease, and transplant-related characteristics are summarized in Table 1. Two hundred forty-two patients with a median age of 48 years (range, 18 to 71) underwent transplantation. One hundred twenty-three patients were male (51%), and peripheral blood stem cells were used in 178 patients (74%). Donors were matched related (n = 155, 64%) or matched unrelated (n = 87, 36%). Median follow-up of survivors was 65 months (range, 12 to 145).

The number of patients in each of the 4 groups based on age and remission status as previously defined was as follows: 116 patients (48%) transplanted in CR1 age <60, 78 patients (32%) in CR2 age <60, 32 patients (13%) in CR1 age ≥60, and 16 patients (7%) in CR2 age ≥60. Among the study patients, 170 (70%) received myeloablative conditioning regimens and 72 patients (30%) RIC regimens. Of the 48 patients ≥60 years of age, 46 (96%) received RIC regimens. Of the 194 patients <60 years of age, 26 (13%) received RIC regimens.

Primary Endpoints

Overall survival

Univariate comparison between the 4 groups divided by age/remission status (<60 in CR1, <60 in CR2, ≥60 in CR1, and ≥60 in CR2) demonstrated a significant difference in survival ($P = .003$) (Figure 1a). OS at 3 years for the 4 groups was 57% (95% confidence interval [CI], 48% to 66%), 43% (95% CI, 32% to 54%), 39% (95% CI, 22% to 56%), and 16% (95% CI, 3% to 38%), respectively. The hazard ratios (HRs) for survival for the groups <60 CR1, <60 CR2, and ≥60 CR2 compared with group ≥60 CR1 were .67 ($P = .13$), 1.03 ($P = .91$), and 1.83 ($P = .08$), respectively. Of the other variables studied, unrelated donor status carried an increased risk ($P = .04$; HR, 1.44) and an HCT-comorbidity index score ≥3 ($P = .02$; HR, 1.55). In the univariate analysis, cytogenetic risk at diagnosis, gender, cytomegalovirus serostatus, graft source, conditioning intensity, and year of transplant during/after 2006 were not statistically significant for OS.

A limited multivariable analysis was performed for OS using the parameters age/remission status, donor type, conditioning regimen, HCT-comorbidity index score, and year of transplant during/after 2006. Age/remission status group had a significant effect on OS (overall $P = .02$). HRs for the groups <60 CR1, <60 CR2, and ≥60 CR2 in reference to group ≥60 CR1 were .47, .61, and 1.52, respectively. Transplant performed during/after 2006 influenced OS favorably ($P = .04$; HR, .67). Donor status, conditioning regimen, and

Table 1
Baseline Patient, Disease, and Transplant-Related Characteristics as Well as Comparison of Distributions of These Characteristics among 4 Groups Defined by Age and Remission Status

Characteristics	All Patients (N = 242)	Age <60 CR1 (n = 116)	Age <60 CR2 (n = 78)	Age ≥ 60 CR1 (n = 32)	Age ≥ 60 CR2 (n = 16)	*P*
Age, median in years (range)	48 (18-71)	44 (18-59)	45 (18-59)	63 (60-71)	65.5 (60-70)	
Gender						.35
Male	123 (51%)	60 (52%)	37 (47%)	20 (63%)	6 (37%)	
Female	119 (49%)	56 (48%)	41 (53%)	12 (37%)	10 (63%)	
HCT-comorbidity index score						.0002
0-2	171 (70%)	95 (82%)	45 (58%)	24 (75%)	7 (44%)	
≥3	71 (30%)	21 (18%)	33 (42%)	8 (25%)	9 (56%)	
Cytogenetic risk*						.15
Favorable	18 (7%)	8 (7%)	9 (11%)	0 (0%)	1 (6%)	
Intermediate	107 (44%)	50 (43%)	31 (40%)	17 (51%)	9 (56%)	
Unfavorable	55 (23%)	32 (28%)	14 (18%)	8 (25%)	1 (6%)	
Unknown/ND	62 (26%)	26 (22%)	24 (31%)	7 (22%)	5 (31%)	
Graft						<.0001
Bone marrow	64 (26%)	36 (31%)	28 (36%)	0 (0%)	0 (0%)	
Peripheral blood	178 (74%)	80 (69%)	50 (64%)	32 (100%)	16 (100%)	
CMV donor/recipient						.51
Neg/neg	78 (33%)	38 (33%)	28 (37%)	9 (28%)	3 (19%)	
Others	160 (67%)	77 (67%)	47 (63%)	23 (72%)	13 (81%)	
Donor type						<.0001
Related	155 (64%)	93 (80%)	27 (35%)	27 (84%)	8 (50%)	
Unrelated	87 (36%)	23 (20%)	51 (65%)	5 (16%)	8 (50%)	
Conditioning intensity						<.0001
MAC	170 (70%)	103 (89%)	65 (83%)	2 (6%)	0 (0%)	
RIC	72 (30%)	13 (11%)	13 (17%)	30 (94%)	16 (100%)	
HCT year						.001
Before 2006	147 (61%)	84 (72%)	42 (54%)	16 (50%)	5 (31%)	
2006 or after	95 (39%)	32 (28%)	36 (46%)	16 (50%)	11 (69%)	

ND indicates not determined; CMV, cytomegalovirus; MAC, myeloablative conditioning.
* At diagnosis as defined by Southwest Oncology Group/Eastern Cooperative Oncology Group criteria [13].

HCT-comorbidity index score had no significant effect (Table 2).

Leukemia-free survival

A univariate comparison between the 4 groups divided by age/remission status (<60 in CR1, <60 in CR2, ≥60 in CR1, and ≥60 in CR2) demonstrated a significant difference in LFS between the respective groups ($P = .0005$) (Figure 1b). The HRs for LFS for the groups <60 CR1, <60 CR2, and ≥60 CR2 compared with group ≥ 60 CR1 were .60 ($P = .04$), .96 ($P = .87$), and 1.74 ($P = .09$), respectively. Concerning the other variables studied, only an HCT-comorbidity index score ≥ 3 demonstrated a marginally significant impact ($P = .04$; HR, 1.4; 95% CI, 1.02 to 2.03). LFS at 3 years for the 4 groups was 57% (95% CI, 48% to 66%), 37% (95% CI, 26% to 48%), 34% (95% CI, 18% to 50%), and 13% (95% CI, 2% to 33%), respectively (Figure 1B).

Multivariable analysis performed for LFS was based on age/remission status, donor type, conditioning regimen, HCT-comorbidity index score, and year of transplant during/after 2006. LFS was significantly influenced by age/remission status group ($P = .02$). HRs for the groups <60 CR1, <60 CR2, and ≥60 CR2 in reference to group ≥60 CR1 were .46, .66, and 1.51, respectively. The other variables had no significant effect on LFS (Table 2).

Nonrelapse mortality

The 3-year cumulative incidence of NRM in the 4 groups was 29% (95% CI, 20% to 38%), 38% (95% CI, 26% to 51%), 31% (95% CI, 8% to 55%), and 63% (95% CI, 31% to 94%), respectively ($P = .04$) (Figure 2A). The HR for NRM for the group ≥60 CR2 compared with group ≥60 CR1 was 2.1 ($P = .02$). In the univariate analysis, other factors associated with high NRM

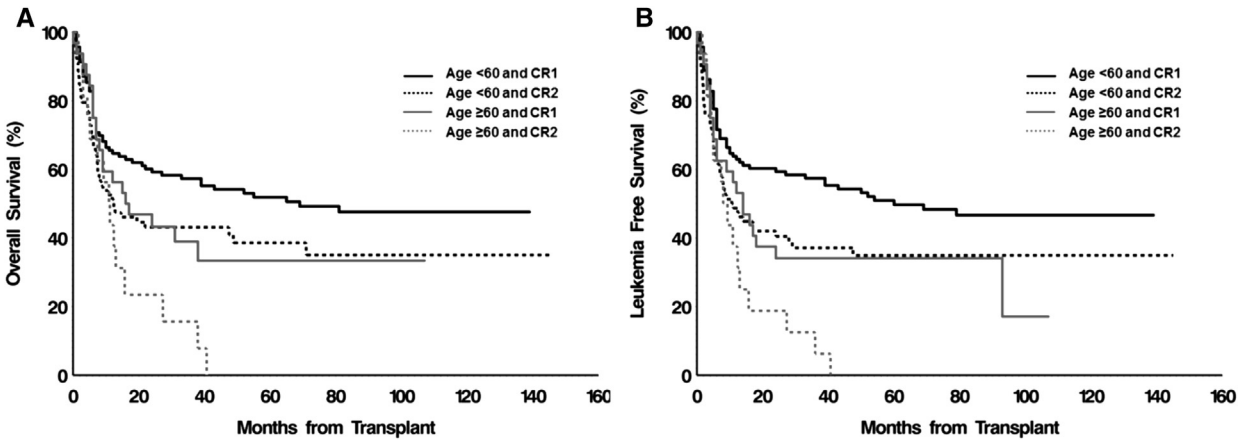

Figure 1. (A) OS after univariate analysis, stratified by CR status and age ($P = .003$). (B) LFS, stratified by CR status and age ($P = .0005$).

Table 2
Multivariable Analysis for OS, LFS, CIR, and NRM

	HR	95% CI	*P*
OS			
Age/CR status			.02 (overall)
<60/CR1	.47	.23-.95	.03
<60/CR2	.61	.29-1.28	.19
≥60/CR1	1.00	—	—
≥60/CR2	1.52	.76-3.04	.23
Donor			
Related	1.00	—	
Unrelated	1.50	.99-2.26	.05
Regimen			
MAC	1.00	—	
RIC	.75	.43-1.30	.31
HCT-comorbidity index			
0-2	1.00	—	
≥3	1.36	.93-1.97	.11
HCT year			
Before 2006	1.00	—	
2006 or after	.67	.46-.99	.04
LFS			
Age/CR status			.02 (overall)
<60/CR1	.46	.23-.91	.03
<60/CR2	.66	.32-1.35	.25
≥60/CR1	1.00	—	—
≥60/CR2	1.51	.77-2.94	.23
Donor			
Related	1.00	—	
Unrelated	1.34	.89-2.00	.16
Regimen			
MAC	1.00	—	
RIC	.82	.47-1.41	.46
HCT-comorbidity index			.27
0-2	1.00	—	
≥3	1.23	.85-1.77	
HCT year			.09
Before 2006	1.00	—	
2006 or after	.72	.50-1.05	
CIR			
Age/CR status			.98 (overall)
<60/CR1	1.03	.39-2.70	.95
<60/CR2	1.61	.62-4.16	.33
≥60/CR1	1.00	—	—
≥60/CR2	.90	.33-2.41	.83
Donor			.20
Related	1.00		
Unrelated	.67	.36-1.24	
Regimen			.01
MAC	1.00		
RIC	2.88	1.33-6.21	
HCT-comorbidity index			.34
0-2	1.00		
≥3	.73	.39-1.38	
HCT year			.17
Before 2006	1.00	—	
2006 or after	1.43	.85-2.40	
Cumulative incidence of NRM			
Age/CR status			.01 (overall)
<60/CR1	.32	.13-.80	.01
<60/CR2	.38	.15-.99	.05
≥60/CR1	1.00	—	—
≥60/CR2	2.08	.98-4.41	.06
Donor			
Related	1.00	—	
Unrelated	1.91	1.11-3.26	.02
Regimen			.01
MAC	1.00	—	
RIC	.33	.16-.70	
HCT-comorbidity index			.13
0-2	1.00	—	
≥3	1.42	.91-2.24	
HCT year			.01
Before 2006	1.00	—	
2006 or after	.43	.26-.71	

MAC indicates myeloablative conditioning.
Dashes indicate the reference group which the other groups within the variable are compared to.

were use of unrelated donors ($P = .04$; HR, 1.53; 95% CI, 1.01 to 2.32) and an HCT-comorbidity index score ≥3 ($P = .03$; HR, 1.63; 95% CI, 1.06 to 2.51). Year of transplant during/after 2006 was associated with less NRM ($P = .02$; HR, .60; 95% CI, .38 to .93).

Multivariable analysis (using the previously mentioned for OS and LFS parameters) showed that age/remission status group had a significant effect on NRM (overall $P = .01$; HR for ≥60 CR2 was 2.08 in reference to group ≥ 60 CR1, $P = .06$). Use of RIC regimens was associated with significantly decreased NRM ($P = .01$; HR, .33), as was transplant performed during/after 2006 ($P = .01$; HR, .43). Unrelated donor transplant was associated with increased NRM ($P = .02$; HR, 1.91) (Table 2).

Relapse

In a univariate analysis, 3-year CIR in the 4 groups were 14% (95% CI, 6% to 22%), 24% (95% CI, 10% to 39%), 34% (95% CI, 14% to 55%), and 31% (95% CI, 10% to 56%), respectively ($P = .05$) (Figure 2b). The HR for CIR for the group ≥ 60 CR2 compared with group ≥ 60 CR1 was .78 ($P = .63$). Univariate analysis demonstrated use of RIC regimens to be associated with a significant increase in CIR ($P < .01$; HR, 2.6; 95% CI, 1.52 to 4.29). Multivariable analysis (using the previously mentioned for OS, LFS, and NRM parameters) showed that age/remission status group had no significant effect on CIR (overall $P = .98$), whereas RIC regimens were associated with significantly increased CIR ($P = .01$; HR, 2.88) (Table 2).

Causes of Poor Outcome in Patients ≥60 Years in CR2

We attempted to study in detail the reasons for poor outcome in patients aged ≥60 years in CR2 by a detailed chart review (n = 16) (Table 3). We were particularly interested in understanding whether those transplants could have been performed in CR1. Of the 16 patients transplanted in CR2, 9 patients were not referred for transplant in CR1. Of the remaining 7 patients, there was no indication for transplant in CR1 in 2 patients as per established indications for transplant in our program, 1 patient refused transplant in CR1, and 4 patients relapsed while waiting for transplant.

DISCUSSION

With the availability of RIC in the last 15 years, allogeneic transplants in older patients with AML has been increasingly used [1]. Although several prospective studies have demonstrated the benefit of transplant over conventional chemotherapy in younger patients in CR1, such prospective comparative data in older patients are not available. Several single-center and large registry–based studies have demonstrated the feasibility and efficacy of allogeneic transplantation in older patients with AML. However, which older patients are likely to benefit from allogeneic transplants is not entirely clear. In the absence of prospective comparative data of allogeneic transplants versus conventional chemotherapy alone, many centers use similar indications for transplant as those used in younger patients.

In this study, we evaluated and compared the outcomes of older patients with younger patients based on remission status. We demonstrate that HCT can produce long-term disease control and possibly cure in about one third of patients ≥60 years in CR1; however, such benefit was lacking in older patients in CR2. None of the patients transplanted in CR2 survived in the long term. The main cause of failure in older patients in CR2 was high NRM, and the HR for NRM was >2 times compared with older patients in CR1

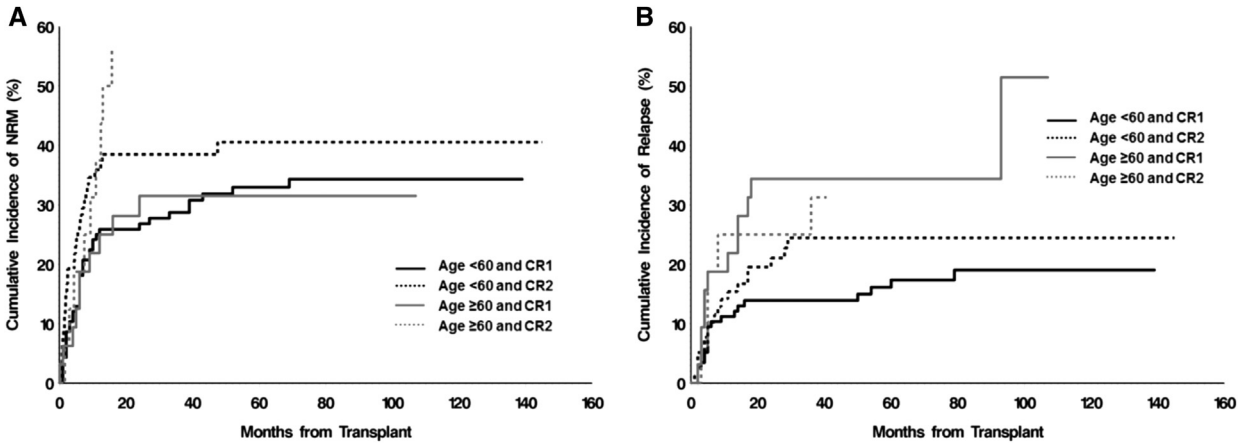

Figure 2. (A) Cumulative incidence rate of NRM, stratified by CR status and age ($P = .04$). (B) CIR rate, stratified by CR status and age ($P = .05$).

(Table 2). Older patients are more vulnerable to organ damage resulting from multiple rounds of intensive chemotherapy as well as infectious complications. Our data also show that burden of comorbidities increases with disease beyond CR1. The proportion of patients with HCT-comorbidity index score ≥ 3 in age < 60 years CR1, age ≥ 60 years CR1, age < 60 years CR2, and age ≥ 60 years CR2 was 18%, 25%, 42%, and 56%, respectively (Table 1). This may partially explain the high NRM in older patients in CR2, because an increased HCT-comorbidity index score has been associated with worse outcomes for AML in CR2 [12]. On the other hand, selected older patients with a low HCT-comorbidity index score have demonstrated the feasibility of transplant in an older AML population, although most of these patients underwent HCT in CR1 [19].

We also tried to explore the reasons for older patients undergoing transplant in CR2. One of the main reasons was that some patients were not referred for transplant in CR1. Some physicians are still reluctant to refer older patients for transplant in CR1. We recommend that the option of transplant should be offered to appropriate older patients in CR1, and the decision to proceed or defer transplant in CR1 should be made after consultation with a transplant center. The second important cause in our dataset was disease relapse while waiting for transplant. This indicates the need for urgent transplantation because remissions may not be durable in some patients. With the increasing utilization of transplant services, there has been a tremendous strain on health care resources. Challenges have been seen in the capacity-building issues to funding and human resources. With the increase in the aging population, these issues will have to be addressed in a meaningful way so for eligible patients the option of transplant can be provided in a timely fashion. Alternative graft sources in older patients such as cord blood [20] or haploidentical donors may prove to be useful in the setting of a clinical trial.

A question arises from these data: Should older patients in CR2 be denied the option of transplant? We recommend caution in the interpretation of these data, because they are not sufficient in denying this option. However, these data are

Table 3
Detailed Characteristics of the 16 Patients Aged ≥ 60 Years Transplanted in CR2

Patients (n = 16)	Age	Cytogenetic Risk*	Primary vs. Secondary AML	Donor Type	Duration CR1 (mo)	Reason Transplant Not Performed in CR1	HCT-Comorbidity Index Score	Time to Death (mo)	Cause of Death Post-Transplant
1	60	Intermediate	Primary	MUD	16	Not referred	4	11	GVHD
2	60	Intermediate	Primary	Related	17	Not referred	5	2	GVHD
3	62	Intermediate	Primary	MUD	61	Not referred	3	16	Aspergillosis, GVHD
4	62	Unknown	Primary	Related	4	Relapsed while waiting for HCT	1	27	Pneumonia
5	63	Intermediate	Primary	Related	8	Patient refused HCT in CR1	1	17	Relapse
6	64	Intermediate	Primary	MUD	80	Not referred	4	7	Graft failure
7	64	Unavailable	Secondary	Related	15	Not referred	3	9	Metastatic breast cancer
8	65	Unavailable	Secondary	MUD	6	Relapsed while waiting for HCT	4	3	Relapse
9	66	Favorable	Primary	Related	22	Favorable cytogenetics	0	13	NRM related to progressive parkinsonism
10	66	Intermediate	Primary	MUD	16	Favorable molecular profile	2	12	Sepsis
11	66	Unavailable	Secondary	Related	14	Not referred	3	41	Cardiac
12	67	Intermediate	Primary	Related	4	Relapsed while waiting for HCT	0	38	Relapse
13	68	Unfavorable	Primary	MUD	4	Relapsed while waiting for HCT	2	5	Relapse
14	69	Intermediate	Primary	MUD	64	Not referred	3	4	Sepsis
15	70	Intermediate	Primary	Related	8	Not referred	1	11	Relapse
16	70	Unknown	Primary	MUD	56	Not referred	4	3	Sepsis

MUD indicates matched unrelated donor; GVHD, graft-versus-host disease.
* Southwest Oncology Group/Eastern Cooperative Oncology Group criteria [13].

more suggestive of the possibility of improving outcomes by early referral of eligible older patients for transplant. Patients who are unlikely to benefit from transplant should be enrolled in novel clinical trials, and several new encouraging approaches are in progress in patients with AML.

In summary, our data demonstrate that patients ≥ 60 years with AML in CR1 derive benefit from the curative potential of HCT. However, mainly due to high NRM, patients ≥60 years in CR2 would have to be carefully selected with minimal comorbidities if any benefit is to be expected with HCT. Close collaboration between leukemia physicians and transplant centers is needed, and if HCT is indicated in patients ≥60 years, attempts should be made to deliver the transplant in CR1.

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